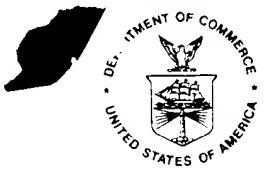

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	14

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/872,527	Guo
Examiner	**Art Unit**
Marianne DiBrino	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on Apr 3, 2001

2a) ☐ This action is **FINAL.** 2b) X This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) X Claim(s) 103-139 is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed

6) X Claim(s) 103-139 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d)

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) X Interview Summary (PTO-413) Paper No's. 23

19) ☐ Notice of Informal Patent Application, PTO-152

20) ☐ Other

DETAILED ACTION

1. Applicant's amendment, filed 4/3/01 (Paper No. 22), is acknowledged and has been entered.

Claims 103-139 are pending and are presently being examined.

The following are new grounds of rejection.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Applicant is reminded of the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999; the following rejection is set forth herein.

Claims 103-139 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed composition comprising antibodies with one or more antigen binding sites for one or more gp55 antigens on the surface of one or more target hepatocellular carcinoma, lymphoma or colorectal carcinoma cells.

The instant claims encompass antibodies which have antigen binding sites for any glycoprotein antigen on the surface of the said target cells which is of the size 55 kDa, i.e., "gp55". There is insufficient disclosure in the specification on such said blocking agent.

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli , 872 F.2d 1008, 1012, 10 USPQ2d

1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood , 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of an antigen "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description ... requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; Id. at 1170, 25 USPQ2d at 1606.

The instant specification discloses (on page 5 at lines 23-27 and continuing on to page 6 at lines 1-14) that weakly or non-immunogenic autologous target cells are treated in order to amplify primary and costimulatory T cell activation signals in the cells, and bispecific monoclonal antibodies capable of binding to one or more antigens on the treated cells and to one or more T cell activation costimulatory molecules on the surface of T cells are attached. The instant specification discloses that "target diseased cell" is a cell causing , propagating, aggravating or contributing to a disease (page 8 at lines 18-20). The instant specification discloses (on pages 37-39 and 40-42) use of the invention to cause hepatoma tumor cell regression in mice and to cause tumor regression of EL-4 lymphoma and SMCC-1 colon carcinoma in mice, respectively. The specification further discloses that three monoclonal antibodies were produced which reacted with hepa 1-6 cells and recognized either a 55 kDa, 95 kDa or 210 kDa glycoprotein expressed on most tumor cells as determined by immunoprecipitation. The specification discloses that the said monoclonal antibodies were designated as anti-gp55, anti-gp95 and anti-gp210, respectively (page 32 at lines 8-20). The specification also discloses that bispecific monoclonal antibodies were produced from these antibodies (page 33 at lines 4-6).

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. However, a generic statement such as "gp55", without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by the property of being a glycoprotein of 55 kDa size. It does not specifically define any of the glycoproteins that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others, other than size. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity

of the members of the genus. Many such species may be 55 kDa in size. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin [e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

Since the disclosure fails to provide sufficient relevant identifying characteristics that identify members of the genus, and given the broad genus claimed, the disclosure of an antibody to a protein of 55 kDa on the surface of one type of hepatocellular carcinoma cell line is insufficient to describe the genus as broadly claimed. One of skill in the art would not have recognized that Applicant was in possession of the invention claimed in the instant claims.

4. Claims 103-139 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not disclose how to make and/or use the instant invention. The claimed composition comprising one or more isolated autologous target hepatocellular carcinoma, lymphoma or colorectal carcinoma cells and one or more antibodies comprising one or more binding sites for one or more gp55 antigens on the surface of one or more of the autologous target cells encompasses: (1) making and using antibodies to any 55 kDa glycoprotein, i.e., "gp55", on the surface of any isolated autologous target hepatocellular carcinoma, lymphoma or colorectal carcinoma cell, and (2) making and using a composition comprising an isolated autologous target cell that has not been irradiated. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass a composition which comprises an antibody with a specificity against any cell surface protein on an isolated autologous target cell recited in the instant claims. The state of the art is such that it is unpredictable in the absence of appropriate evidence whether the claimed compositions can be made and/or used. The specification discloses working examples of compositions comprising HEPA 1-6 hepatocellular carcinoma cells, EL-4 lymphoma cells and SMCC-1 colon carcinoma cells, said cells being armed with anti-CD28:gp55 monoclonal antibody (Examples 6.2-6.7) and use in mice. The specification discloses no working examples with regards to the use of the instant invention (i.e., non-irradiated tumor cells) for treating of cancer in vivo in humans or in any mammal.

The instant specification discloses (on page 5 at lines 23-27 and continuing on to page 6 at lines 1-14) that weakly or non-immunogenic autologous target cells are treated in order to amplify primary and costimulatory T cell activation signals in the cells, and bispecific monoclonal antibodies capable of binding to one or more antigens on the treated cells and to one or more T cell activation costimulatory molecules on the surface of T cells are attached. The instant specification discloses that "target diseased cell" is a cell causing, propagating, aggravating or contributing to a disease (page 8 at lines 18-20). The instant specification discloses (on pages 37-39 and 40-42) use of the invention to cause hepatoma tumor cell regression in mice and to cause tumor regression of EL-4 lymphoma and SMCC-1 colon carcinoma in mice, respectively. The specification further discloses that three monoclonal antibodies were produced which reacted with hepa 1-6 cells and recognized either a 55 kDa, 95 kDa or 210 kDa glycoprotein expressed on most tumor cells as determined by immunoprecipitation. The specification discloses that the said monoclonal antibodies were designated as anti-gp55, anti-gp95 and anti-gp210, respectively (page 32 at lines 8-20). The specification also discloses that bispecific monoclonal antibodies was produced from these antibodies (page 33 at lines 4-6).

The specification does not appear to disclose irradiation of the target tumor cells prior to in vivo treatment.

The specification does not disclose that the said monoclonal antibody against a 55 kDa glycoprotein on HEPA 1-6 cells is readily available to the public, nor does the specification disclose a repeatable method for obtaining the said monoclonal antibody. It is apparent that the said antibody is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. There is no disclosure in the specification of the particular epitope, nor the sequence of the protein recognized by the said antibody, and therefore a routineer would not be able to produce said antibody based on the disclosure of the specification. If the said antibody is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the hybridoma producing the said antibody. See 37 CFR 1.802.

Evidentiary reference U.S. Patent No. 5,484,596 (of record) discloses using irradiated tumor cells as a vaccine in order that the tumor cells are viable but not tumorigenic (especially Abstract). Evidentiary reference Periera et al teach "GP55" which is a viral envelope glycoprotein from SFFV (spleen focus forming virus) required for leukemogenicity (especially page 5106), i.e., the "GP55" of Periera et al is an example of a viral glycoprotein that is tumorigenic and is of the same size as the "GP55" protein on the surface of HEPA 1-6 cells in the instant specification, but which may be a different glycoprotein.

For these reasons, it is not clear that reliance on the use of non-irradiated tumor cells of the invention to treat mice accurately reflects the relative efficacy of the therapeutic strategy of treating any mammal, including human, using non-irradiated tumor cells.

There is insufficient guidance in the specification as to how to make and/or use the instant invention, including reliance on a monoclonal antibody made to a glycoprotein of 55 kDa on the surface of the HEPA 1-6 hepatocellular carcinoma cell line. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

The following are new grounds of rejection necessitated by Applicant's amendment filed 4/3/01.

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 103-139 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 70-110 of copending Application No. 09/216,062. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are encompassed by the said claims of the '062 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims are not patented.

7. Claims 123, 124 and 125 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amendatory material not supported by the disclosure as originally filed is as follows: "wherein over 90% of said antibodies are attached"(claim 123) and "wherein over 95% of said antibodies are attached" (claim 124) and "substantially free" (claim 125). Applicant does not point to support in the originally filed disclosure.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 103-139 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 125 is indefinite in the recitation of "substantially free" because it is not clear what the metes and bounds of the said phrase are.

b. Claims 103-139 are indefinite in the recitation of "wherein said one or more antibodies further comprise one or more antigen binding sites for one or more gp55 antigens on the surface of said one or more target hepatocellular carcinoma, lymphoma or colorectal carcinoma cells" because the characteristics of the said gp55 antigens and hence, that of the said antibodies, are not known. The use of "gp55" as the sole means of identifying the protein to which the claimed antibody is specific renders the claim indefinite because "gp55" is merely a laboratory designation which does not clearly define the claimed product, since the said designation is merely a characterization of a protein by size and may refer to many different proteins.

10. No claim is allowed.

11. This action is made NON-final.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne DiBrino whose telephone number is (703) 308-0061. The examiner can normally be reached Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Marianne DiBrino, Ph.D.
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June 8, 2001

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